ON THE PROGRESS
OF
SCIENTIFIC PATHOLOGY.

AN ADDRESS
DELIVERED AT
THE OPENING OF THE SECTION OF PATHOLOGY,

At the Annual Meeting of the
British Medical Association, held in Glasgow, August 1888.

BY

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ON THE PROGRESS OF SCIENTIFIC PATHOLOGY.

To have been invited to preside over the Section of Pathology at this important annual meeting of our Association in this famous city, is, for me, a very great honour. And, in spite of an overpowering consciousness of inefficiency to discharge the duties of a president from sheer inexperience in such duties, I nevertheless accepted the position, because in the selection made by your Council I consider that a compliment has been paid to the Army Medical School at Netley, to which I have the honour to belong, not less than to myself.

Nevertheless, I feel the responsibility of venturing to follow those distinguished men who have year by year from this chair addressed the Sections in Pathology—men whose names are famous throughout the world for their genius, their talents, and their culture. But I am encouraged to undertake the duty believing that I can rely upon your indulgence and upon the able assistance of my friends who are associated with me as Vice-Presidents and Secretaries of the Section.

Personally, it is a great gratification to me to occupy this position, because of my previous connection with the ancient University of this great city, in which I had formed friendships that have never ceased to be, for me, a source of the most pleasant recollections. My remembrances of this University are of "long ago"—forty years ago—(1848), when I became associated as Demonstrator of Anatomy with one of its most distinguished professors—the late Dr. Allen Thomson—the memory of whose name must be ever cherished by the thousands of pupils he helped to teach, not less than by his colleagues, who are still left to add lustre to the University of Glasgow.

My first duty, therefore, is respectfully to acknowledge and to express thus publicly my personal appreciation of this distinction, and to thank the members of your Council for an opportunity of revisiting this ancient city under such auspicious circumstances.

I would here also speak a word of welcome, in the name of this Section, to our foreign friends, many of whom have come long distances to take part in its work. We feel highly honoured that men so distinguished in pathology should be with us to-day—men whose names are not only "familiar as household words" in their own country, but of world-wide reputation wherever pathology is studied as a science.

The object of the British Medical Association, throughout all its Sections, is "to promote the progress of medicine;" and in this respect its combined work may be said to have a practical rather than a purely scientific aim. But in this Section of Pathology (as a branch of biology) the Association finds a link which immediately connects it with the science side of medicine, as distinguished from the art or practice of our profession; and in the records of pathology, if we seek diligently, we shall find those maxims which will most safely guide us to the rational practice of our art.

But pathology must be studied as a branch of biology, in the widest acceptation of that term; and when medicine is thus thought of as a pure science, it implies a "pathology" which has no more necessary subservience to practical ends than zoology or botany. The logical connection between this purely scientific doctrine of disease or pathology and ordinary biology has been traced out by the master-mind of Professor Huxley, and expressed in these words: "Living matter is characterised by its innate tendency to exhibit a definite series of the morphological and physiological phenomena which constitute organisation and life. Given a certain range of conditions, and these phenomena remain the same, within narrow limits, for each kind of thing. They furnish the normal and typical character of the species; and, as such, they are the subject-matter of ordinary biology. Outside the range of these conditions, the normal course of the cycle of vital phenomena is disturbed, abnormal structure makes its appearance, or the proper character and mutual adjustment of the functions cease to be preserved. The extent and the importance of these deviations from the typical life may vary indefinitely. They may have no notable influence on the general well-being of the economy, or they may favour it. On the other hand, they may be of such a nature as to impede the activities of the organism, or even to involve its destruction. In the first case, these perturbations are ranged under the wide and somewhat vague category of 'variations;' in the second, they are called 'lesions,' 'states of poisoning,' or 'diseases;' and, as morbid states, they lie within the province of pathology. No sharp line of demarcation can be drawn between the two classes of phenomena. No one can say, for example, where anatomical variations end and tumours begin; nor where modification of function, which may at first promote health, passes into disease. All that can be said is that whatever change of structure or function is hurtful belongs to pathology. Hence it is obvious that pathology is a branch of biology; it is the morphology, the physiology, the distribution, the etiology of abnormal life. Henceforward the connection of medicine with the biological sciences is clearly defined, and pure pathology is that branch of biology which defines the particular disturbances of cell-life, or of the co-ordinating machinery, or of both, on which the phenomena of disease depend."[1]

Our first object, therefore, is to ascertain the laws under which organic bodies live in their usual healthy or normal course of life; on the other hand, we desire to ascertain how those laws come to be altered in an unusual, unhealthy, or abnormal course. When we attempt to do the first of these things, we are physiologists. When we attempt to do the second, we are pathologists;[2] and pathology may be still more concisely described in the words of a veteran and most distinguished pathologist—Sir John Simon—as "a study of the science of life under other conditions than those of ideal perfection."

As to the mode of working in pathology, it is essentially by research—a searching out of the secrets of Nature by experiments. And while such may be described as the very essence of practical pathology, we have also a speculative pathology (too apt at times to run rampant) in which we are constantly tempted to speculate on the nature and origin of diseases, from a most fascinating desire to understand and explain all that we observe. Hence we are tempted to speculate as to the intimate nature, the origin, and essence of the "morbid processes," we have more or less constantly before our eyes, even before we know what these processes really are. By such speculation we seek for and obtain what has been called "a good working hypothesis"—a theory of disease.

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[1] *Science and Culture, and Other Essays*, by T. H. Huxley, LL.D., F.R.S., 1881, p. 326-345.

[2] *History of Civilisation in England*, by Henry Thomas Buckle. 1867 vol. iii, p. 110.

It is only through the agency of practical pathology that we are safeguarded from the errors inherent in all kinds of speculation, and in speculative pathology in particular. Theory and experiment, so long as they go hand in hand, help and check each other; and I think you will agree with me that there never was a time in which there has been greater activity than now in all kinds of pathological work, or more encouragement given to workers in pathology.

Your Association, under its excellent management, has greatly contributed to this activity by the far-seeing organisation through which it has sought to extend the area of original research: 1, by arrangements for the collective investigation of diseases; 2, by its grants in aid to members of the profession engaged in researches for the advancement of medicine and the allied sciences; 3, by the more recent creation of scholarships of research of the annual value of £150 a year, tenable for three years, at any of the suitable schools or laboratories of the British or Continental universities or medical schools.

In all our practical work in pathology we must ever keep in view that it was the great pioneers in physiology who opened its gates for pathology to enter in; and the names of Scheiden and Schwann, Kölliker, Bowman, Goodsir, Allen Thomson, Sharpey, Burdon Sanderson, and Schäfer are familiar to us as the great workers in normal histology. It is the faithful study of normal human histology in British medical schools during the past thirty years which has done so much to promote good pathological work in this country. The establishment of the "cell theory" in physiology was swiftly followed by a "cellular pathology" as its logical counterpart. But it is unquestionably to Virchow that we owe the great advance by which histology came to take a first place as an aid to elemental pathology; and from 1858, the date of the first appearance of his great work on *Cellular Pathology* we may regard as the opening of the present era of modern pathology. This great work, dedicated to John Goodsir "as one of the earliest and most acute observers of cell-life both physiological and pathological," put a new life into pathology. Thus, following in the footsteps of Goodsir, Remak, and other physiologists, it was as a physiologist that Rudolph Virchow gave this great work to the world—a general theory of the relation of the elements of tissue to disease. Starting from the discoveries of Schleiden in 1838 on the cellular structure of the vegetable tissues (which was afterwards put on a sure foundation by Schwann in its application to the animal tissues in 1839), it was shown how, in the cell, is the vital unit of all organised structures, how intimately its changes are associated with all the processes of organic life, both in health and in disease, with the development and maintenance of the tissues, and in all their functional reactions, whether normal or abnormal. In this work Virchow did ample justice to comparative pathology, and to the lessons to be derived from the study of morbid processes, even in plants—as in the comparison he makes of cell growth in the syringa to the proliferation of cartilage. To him, to Sir James Paget, to Pasteur, and to Bland Sutton we are mainly indebted for removing the stigma hitherto attached to us for neglecting the lessons in pathology to be learned from a study of the diseases of plants and animals. It has been found that the comparison of diseases in animal and vegetable life throws much light upon the nature of diseases of man, so that a true and comprehensive human pathology must have a basis in comparative pathology. Philosophers who have had no special acquaintance with our branch of science have been impressed with this truth. Buckle, for example, has thus expressed himself: "The best physiologists distinctly recognise that the basis of their science must include, not only the animals below man, but also the entire vegetable kingdom; and that without the commanding survey of the great realm of organic Nature we cannot possibly understand human physiology, still less general physiology. The pathologists, on the other hand, are so much in arrear that the diseases of the lower animals rarely form part of their plan; while the diseases of plants are almost entirely neglected, although it is certain that until all these have been studied, and some steps taken to generalise them, any pathological conclusion will be eminently empirical on account of the narrowness of the field from which it is collected."[3]

Sir James Paget, in recent years, has most of all helped to exonerate pathologists from this seeming neglect of comparative pathology. It was as a physiologist that he so eloquently expounded the doctrines of an "elemental" pathology at the general meeting of 1880, based on changes seen in the actual elements of the tissues, from numerous and elaborate observations on the diseases of plants—a pathology almost unstudied from a medical point of view—an elemental or cellular pathology, capable of explaining processes common to organisms which possess and organisms which do not possess a nervous system and a circulation, and of explaining those which take place in non-vascular parts, as distinguished from a pathology which refers everything to changes in the blood and to the action of the blood-vessels. And I may here further say that the continuous works of Sir James Paget (like those of Virchow) have marked epochs in English pathology, especially by the publication of his lectures on *Tumours* and those on *Surgical Pathology*, subsequently edited by Sir William Turner—lectures which are essentially those of the blood or vascular pathology, and recognising also inborn or hereditary constitutional disease; and now we have his elemental pathology of plant-life. In this latter direction Sir James Paget has not only indicated a new path in an attractive field of research, but has himself led the way.

Following in the footsteps of Sir James Paget, an important contribution to comparative pathology was published in 1886 by Mr. John Bland Sutton, as *An Introduction to General Pathology*, which shows that much information concerning disease in man can be gained by studying pathology in the lower animals, and that there is much community of disease in them and in man.

Such elemental pathology has been still further advanced by the researches of Mr. W. Roger Williams, Surgical Registrar of the Middlesex Hospital. In his recent work on *The Principles of Cancer and Tumour Formations* (1888) he reviews cell-multiplication and the phenomena of the more complicated types of reproduction, as well as the evolution of vegetable neoplasms. He next describes and discusses animal neoplasms. He lays great stress on the influence of evolution and the ancestry of cells in determining their growth. He thus studies cells in the lower animals and plants in order to compare them with the cells and their mode of growth which form tumours in man, and so proceeds from the study of cells to the study of tissues as combined in the structure of tumours.

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[3] *Loc. cit.*, vol. iii p. 412, new edition, 1867.

The study of elemental cell-life has received a still more recent expansion and embodiment in a splendid physiological essay, *On the Modern Cell Theory, and Theories as to the Physiological Basis of Heredity,* by Professor John G. McKendrick, who gives the address in physiology on Friday next. This question of heredity is one of the most important, alike in physiology and pathology, and at the same time one of the most abstruse; for physiology has not yet opened its gates sufficiently wide to enable us to explain the well established facts of heredity, either as regards normal life, or as regards disease. Professor McKendrick has given a clear and condensed account of the various theories put forward in explanation of it in the light of our present knowledge regarding cells, nuclei, and protoplasm. But in discussing them he finds that not only are they still incapable of explaining all the facts, but to a considerable extent are merely restatements of facts already known. The ultimate problem is still mysterious, and will continue to be so, even if it should be possible in the far off future to trace it to the play of molecular forces; and Mr. Roger Williams notes the influence of evolution and ancestry of cells as of importance in pathology, and suggestive in a scientific point of view as to the hereditary transmission of diseases.

It has now been abundantly shown that all distinctions between physiology and pathology are fictitious and unreal—a position which (following from the teachings of Alison, Allen, Thomson, and Bennett, in Edinburgh; Henlé, in Germany; and Sharpey, in London) has been amply established in various addresses spoken at our Association meetings; notably, in August, 1873, by Professors Dr. George Murray Humphry, Dr. John Burdon Sanderson, the late Dr. Parkes in his address on Medicine; and still more recently in the admirable address of Professor Michael Foster, at the Cambridge meeting of 1880, when he discoursed *On the Relations of Physiology to Pathology.* These are the men who, in this country, above all other men, have done the most to bring physiology and exact inquiry to bear on our knowledge of disease and its treatment. They have shown that "the things we call pathological, are but the deeper strata of the healthy phenomena of life prominently thrust upwards to the surface; functional disturbances placed *en évidence*, by processes which we call diseased, morbid, or pathological, but which are governed and directed by the same fundamental laws which direct the normal processes of life—physiological laws." From this point of view, even physiological teaching is incomplete without the elements of general pathological science in its widest sense, including that of animals and plants; and for this reason, that "the tendency to decadence, disease, degeneration and decay, is just as much an integral part of the living economy as to development, growth, and maturity."

The study of dead matter in morbid anatomy can only guide us up to a certain point. It is living matter with which we have to do. Moreover, it is by the exact study of the phenomena of life, through the science of physiology, that we are able to bridge over the chasm between dead morbid anatomy and living pathology. Practical biology, chemistry, and experimental physiology, combined with the natural history and clinical observation of diseases, are the inseparable adjuncts for working out a scientific pathology; and in proportion as this combined method of working has been recognised, so have been the advances in pathology. It was as a physiologist, working by methods purely physiological that Sir Joseph Lister carried out those remarkable researches which mark an epoch alike in medicine and surgery; on the one hand as regards inflammation, and on the other as regards the circulation of the blood; on which I shall have more to say presently.

As a physiologist Professor Foster has shown that there is but the most superficial distinction to be made between the normal and the abnormal, the healthy and the diseased. The physiologist and pathologist must go hand in hand. Their aims, their subject-matter, and their methods, are essentially the same. Both are building up sciences, partly by observation and partly by experiment. Both find a certain amount of material on which to operate in the every-day phenomena of life which present themselves without interference on our part, and which we call normal on the one hand, or abnormal on the other—the "'irruptive,' the 'explosive,' the 'troublous,' and sometimes the 'terrible' phenomena of disease—in Nature's own experiments."

"But the mere observation of Nature's phenomena of disease may be so few and far between, that a physiology and pathology founded on such observation alone is so slow of development, so uncertain, and with life itself so short, one may not live long enough to see Nature do the experiment which we ourselves might do to-day." A more rapid progress of science, impossible without experiment and at its best but slow, is demanded by human needs. Every student of medicine ought therefore to be well trained at an early period of his career in practical physiological experimental studies, so as to learn under simple conditions the methods and the means of which he may afterwards make use, so as to become practised in the solution of problems identical in their nature with those of disease; but of an easier type, because not overlaid, disguised, or obscured by the "processes of disease," which demand in the first instance a physiological interpretation. Pathology being thus essentially an experimental science, dealing with the same fundamental phenomena as physiology—using the same methods, working in the same spirit, and resolving in the end the same or analagous problems, a special training becomes necessary, which can only be obtained by the establishment of pathological laboratories, fitted up with the proper appliances, wherever researches in pathology are to be carried on. Such laboratories have been fitted up by the College of Physicians in Edinburgh, superintended by our able Secretary, Dr. Sims Woodhead; also by the College of Surgeons in London; at Cambridge, superintended by our Vice-President, Dr. Charles Roy; at Aberdeen, by Dr. Hamilton, and at Edinburgh, by Dr. Greenfield. But every school of medicine must take its share in this labour, if continuous progress is to be made in the science of pathology. Let but the pathologist follow in the footsteps of the biologist, and a great field of labour is open before him. He will go safely from the known to the unknown, guided by the brilliant lamp of the biologist, casting its rays from many luminous centres of light. "No serious advance is made in physiology which is not sooner or later translated into the language of pathology; and no really independent advance is made in pathology which does not either show itself to be in accordance with sound physiological doctrine, or compel the current physiological teaching to widen its doors and admit the new truth."

Professor Michael Foster further points out that the best test of a "new physiological doctrine is that, if true, it will in nearly every case, when properly applied, help to solve some hitherto insoluble pathological problem; and the best criterion of a sound pathological doctrine is that it will stand the ordeal of searching physiological criticism, and show itself in accord with the trustworthy results of independent physiological inquiry. And possibly no function of physiological science is more important than this—namely, of serving as a touchstone by which to try the value (whether true or false) of the pathological theories which flutter down on the pages of our medical literature, thick as the falling leaves of an autumnal day."[4]

In very recent years we have seen how pathology and physiology (human and comparative) have been helps to each other in establishing the doctrine that different parts of the cerebral cortex have different functions. Physiological experiment and the clinical observation of disease—Nature's own experiments—have combined to establish this fact; but it was only by dint of continued experimental inquiry that somewhat contradictory teachings were rectified through the combined experiments of Hitzig, Fritsch, Ferrier, Goltz, and Munck.

In like manner, through clinical observation and experiment a new pathological explanation has recently been given concerning the symptoms and mode of death in a particular class of cases after ovariotomy. Mr. Malcolm, one of the junior surgeons of the Samaritan Free Hospital, London, in a paper read at the Royal Medical and Chirurgical Society of London on October 25th, 1887,[5] has shown by clinical and *post-mortem* evidence how paralysis of the intestines and consequent death may result from exposure and manipulation of the abdominal contents during such an operation. His new explanation of the symptoms and mode of death in such cases is based on our knowledge of the minute anatomy and physiology of the muscular and nervous tissues entering into the structure of the intestines, and especially as a result of the experimental researches of Sigmund Mayer, Von Basch, Schiff, Landois, Nasse, Lister, and other physiologists, who have demonstrated that all kinds of stimuli brought to bear on the intestines produce increased activity, followed (if stimulation be sufficiently prolonged and strong) by paralysis of the muscular tissue of the wall of the gut, through Auerbach and Meissner's plexus of nerves. Intestinal obstruction follows as a result of this paralysis, and becomes a frequent cause of death.

We have every reason to believe, therefore, that "as in the past, so in the future, the truths of physiology will serve, on the one hand, as the starting point of pathological doctrine, and, on the other hand, as a tribunal before which each new pathological theory must be tested at its birth. Hence it becomes necessary that students of medicine should be trained early into good habits of physiological criticism—seeing that the physiological is the true pathological mind."[6]

Here, also, one might show how the altered relations of surgery to medicine, as set forth by Sir William Stokes[7] have tended to further the progress of pathology; and how, as Sir James Paget has shown, "scientific methods have been more fully brought into the study of the principles of our art than ever they were before, so that scientific knowledge has become welded with the lessons of experience." It has been very generally known for some time that a perfectly new surgical success has been won in England and in Scotland, of which as yet we are not able to measure the results. I refer especially to the operations of Dr. William Macewen, of this city, of which he will give an account to-morrow, and of Dr. Gowers and Mr. Victor Horsley, Mr. Godlee, and Dr. Bennett in London. At the concluding meeting of the Royal Medical and Chirurgical Society of London, held on Tuesday, June 12th, 1888, Dr. Gowers and Mr. Horsley detailed the facts of a case in which a tumour of the dura mater of the cord was successfully removed from within the bony canal, with complete recovery of the patient.[8] We shall get accustomed in time, no doubt, to the idea that, under proper conditions of precaution some tumours of the brain may be removed *en masse*, with the gain of life; and now but recently the spinal cord has been laid bare of part of its bony covering, in order that by the surgeon's knife it might be relieved of a tumour pressing upon it. The experiments by Professor Ferrier have now been amply justified both in this country, in France and in America; and with the evidence of the usefulness of experiments on living animals to the human race, it would seem to be a natural consequence that the restrictions under which these are now pursued in this country would be materially relaxed. "Knowledge itself is a benefit to mankind; and all knowledge wrested from Nature will sooner or later be turned to profitable account, both in the enlargement of man's intelligence and in the relief of man's estate. This is the broad ground on which experiments on living animals must in the long run be justified."[9]

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[4] *On the Relation of Physiology to Pathology*, JOURNAL, August, 1880, vol. ii.

[5] Reports of Medical Societies in the medical journals of October 29th, 1887. The pathology of this form of paralysis has since been confirmed by the independent observations of Professor Olshausen (JOURNAL, May, 1888, p. 1073, also *Centralblatt für Gynäkologie*, January 7th, 1888).

[6] Michael Foster, *loc. cit.*

[7] The Cavendish Lecture *On the Altered Relation of Surgery to Medicine*, JOURNAL, June 19th, 1888.

Pathology, like physiology, in spite of the obstacles that block its path by original research and experiments in this country, and the restrictions which thus cripple its efforts, is still a progressive science; and many are the questions and theories of increasing interest and importance for us at the present time, questions and theories which may seem to be transcendental and useless. But relying on the abundant evidence of progress in the past, it may be predicted that the solution of these transcendental questions, or of problems equally beyond our ken in their present aspect, will become in time part and parcel of the known pathology of the future."[10] Living in the present we are often incompetent and always imperfect judges of the value in the future of scientific knowledge, or even of single facts; for every fact in science, wherever gathered, has not only a present value, which we may estimate, but has a living, germinal, potential value, of which none can guess the issue.[11] Let us aspire then to know everything; the limits will come later. In the human family the last to be born are the privileged ones. What a host of things they will know which we can never know! How many problems will be clear for them, the solution of which we would gladly purchase with many years of our lives, if we had them to give!

If I might now shortly indicate the direction in which the greatest advances have been made in pathology during the past thirty years, I should say it lay (1) in a better appreciation of the "processes of disease," (2) in an increasing importance attaching to the many factors which combine to produce disease. In other words, an ever-increasing importance attaches to morbid anatomy, physiology, and etiology.

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[8] JOURNAL, June 16th, 1888.

[9] The *Times*, December 27th, 1884.

[10] Professor Michael Foster: Address in Physiology in BRITISH MEDICAL JOURNAL, vol. ii, 1880.

[11] Sir James Paget, Bart: International Congress Address, JOURNAL, 1881, p. 196, vol. ii.

As to Processes of Disease.—Morbid anatomy has discovered lesions and diseases before unknown, which clinical observation has been able to connect with the symptoms and functional disturbances associated with them, and which notify their existence. New processes of disease have been discovered, and older processes have been better explained and understood. Some pathologists have already accepted it as a fact that certain morbid poisons, the contagia of erysipelas, pyæmia, and tuberculosis, are intimately related to the common ferments of putrefaction; and that the most vehement of those contagia can be developed by the artificial culture of successive transmissions in the living body from the comparatively mild contagium of any common inflammatory process.[12]

Professor Burdon Sanderson's papers also show that the occurrence of tubercle (characterised by more or less well-marked features) may be derived by cultivation[13] from such a common inflammation as that induced by a chemical irritant. It therefore "concerns us to remember that apparently every common inflammatory process includes more or less of textural changes which are necrotic and of septic tendency.[14]

This doctrine of a common disorder acquiring specific power is not a new one, as I hope to be able to show.

Great and important changes in subjects connected with the doctrines of pathology and in morbid anatomy have been gradually brought about in recent years "by the accumulation of facts, and by the collection of truths inferred from facts by successive discoverers;" and so effectually will "truths continue to kindle light for truths."[15] The more prominent and interesting "processes of disease," alike in a scientific and practical point of view, which have in this way received greater elucidation during the past thirty years, may be here referred to. They are especially:—1. Those of Virchow, as regards the phenomena of thrombosis and embolism. 2. The pathological relations of blood pressure as an important factor in "disease processes." Ludwig, by applying the kymograph to the hæmo-dynamometer in 1848, enabled the pressure of the blood to write its own story; and as physiologists, appreciating its vascular mechanism, we have been better able to understand the conditions under which, for example, albumen may appear in the urine and again disappear, and how the excretion of urine may also be increased or diminished. Further, we are able approximately to determine the internal pressure which the blood is exercising on the walls of the capillaries and on the minute arteries and veins by studying and determining the effects of "peripheral friction" and "peripheral resistance." As physiologists, by a knowledge of "blood pressure," we can appreciate how some diseases of the heart and circulatory system are brought about; and in connection with investigations on "blood-pressure" I beg leave to connect the name of Dr. Roy of Cambridge, one of our vice-presidents. 3. I would name the phenomena of "inflammation," especially in the structural changes of the minute tissue elements and of the vascular phenomena. The results are in a great measure due to the experiments and observations of Sir Joseph Lister, Virchow, and his pupil von Recklinghausen, and to Cohnheim. They have especially studied the effects of irritation on the vascular and extravascular elements of the tissue; and their results show that in inflammation the functional, nutritive, and formative properties of the tissues are gravely and essentially implicated. They have shown that the process is one in which many phases of morbid action are passed through, finishing by the exudation not only of liquor sanguinis, but by the permeation of the walls of the blood vessels of the inflamed part by the white and red corpuscles of the blood into the surrounding tissue, and without rupture of the blood vessels. More than thirty years ago the beautiful experiments and observations of Sir Joseph (then Mr.) Lister, Professor of Clinical Surgery in King's College, London paved the way for appreciating the phenomena of inflammation as they have since been demonstrated. He clearly showed that a suspension of the concurrent exercise of function among the minute elements of the tissue involved is the primary lesion in the hyperæmia of inflammation. As a rule it precedes stasis, and immediately leads to such derangement of the blood that, in the vicinity of the impaired tissue elements, it tends to assume the same characters as blood always assumes when it is in contact with ordinary solid matter, and renders it unfit for transmission along the course of the blood-vessels. But a return of the tissue elements to their usually active state will be associated with a restoration of the blood to the healthy characters which adapt it for circulation.[16]

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[12] Quain's *Dictionary of Medicine.* Art. "Contagion," by Sir John Simon, vol. i. p. 292.

[13] *Reports of the Medical Officers of the Privy Council for 1868 to 1877*, by Dr. Burdon Sanderson.

[14] Holmes's *System of Surgery.* Art. "Inflammation.".

[15] *Lucretius*, Book I, 1600.

The distinguished German pathologist, Professor Virchow, has since taught us to distinguish two classes of inflammation, in one of which the changes consist in an increased nutritive activity, the implicated tissues themselves taking up a large proportion of nutriment. These he named "parenchymatous" inflammations as distinguished from the other form in which an increase of secretion occurs, and to which he has given the name of "secretory." The cornea and cartilages, the liver, the kidneys, the solid organs generally, and the connective tissue are subject to the first of these forms, while the mucous and serous membranes are commonly the seats of "secretory" inflammation.

In 1867 and 1868, Cohnheim described the transit or permeation of white and red blood cells through the unruptured walls of the capillaries. But the phenomena which Cohnheim described in 1867 had been discovered long before. That these observations had been disregarded so long is another striking instance of the want of appreciation at the time of a cardinal fact of which so many examples are to be found in the history of all sciences.

So long ago as from 1832 to 1842, Dr. William Addison, of Brighton, had perfectly described the emigration of the white blood cells, as well as many other phenomena which attended inflammation. His observations are to be found recorded in the *Transactions of the Provincial Medical Association* for 1842 (now worthily supplanted by THE BRITISH MEDICAL JOURNAL). In other writings he had already shown that white corpuscles not only accumulate in the vessels of inflamed parts, and adhere to their walls, but that they seem to become incorporated with the substance of the vessel, and to pass through it (without permanent solution of continuity) into the surrounding tissue, where they constitute the corpuscles of inflammatory lymph, pus or mucus. The red corpuscles act in the same way. Similar observations were independently made and recorded by Dr. Augustus Waller in vol. xxix of the *Philosophical Magazine.* But Cohnheim's observations went a little farther. He found that these corpuscles may even migrate to some distance from the vessel through which they have permeated, having a power of spontaneous movement by various changes of form, as by sending out processes, blunt or thread-like, to be again withdrawn and the spheroidal form resumed. Thus, by repetitions of these changes of form, the blood corpuscles change from place to place after permeating or passing through the walls of the blood vessels as a swimmer passes through a fluid without leaving a trace of his way. Cohnheim believed, as did Addison and Waller, that the white corpuscles become pus cells. Dr. Charles Williams, in his well-known work on the *Principles of Medicine*, was the first to appreciate the importance of Addison's discovery; but, with regard to practical medicine, the discovery remained a dead letter, so that when Cohnheim reannounced the fact and redescribed the phenomena twenty-eight years later, it came as a surprise and a novelty upon the world of pathology.

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[16] *Royal Society's Proceedings*, June 18th, 1857.

Two important things have thus within the past thirty years been slowly demonstrated since Addison's observations on the phenomena of inflammation in 1832, namely, first, the yielding permeability of the soft, nucleated protoplasm which forms the walls of the living capillaries; and, secondly, the spontaneous amœboid movements possessed by the corpuscles of the blood. Professors von Recklinghausen, in Berlin, Burdon Sanderson, and Bastian, University College, London, have each confirmed these observations in more recent years.

Here, again, we have "a collection of truths inferred from facts by successive physiological discoverers," and the pathology of inflammation seems now to be settling itself on a mixed humoral and solid basis. The albumen in the blood which feeds the organs varies in its nature, and partakes of the quality of the food which supplies it, while it is also modified by the condition of the organs whose actions prepare it for introduction into the current of the blood. The composition of the blood-albumen is thus shown to vary much, and while degrees of nutritive adaptability may exist in it, it is possible that it may be sometimes so degraded as to justify the idea of crases, and may thus again give support to the doctrine of the Vienna school, that every disease implies a dyscrasia, and that alteration of the fluids, and especially of the blood, underlies most morbid changes. But it has now become clear that the main phenomena of nutrition (normal and abnormal) rest with the cells, and that a much larger interpretation must be given alike to the structure of the cell and to the physiology of cell life. To this extent the cellular pathology of Virchow has been a valuable generalisation, and it will be seen how all these recent facts have an important practical bearing on the modern treatment of inflammations.

In addition to the powers possessed by the leucocytes, of effecting a change of place and form, they have also been more recently shown to possess the power of removing foreign matters, combined with the power of "intra-cellular" digestion. The researches of Allman and Meschnikoff have helped to confirm the possession of this power by the cell, and to illustrate or explain also the occasional formation of giant cells in pathological formation. In this way some parasitic existences come to be destroyed by the action of living cells, and the cells which perform the function of eating up other living organisms have received the name of "phagocytes." No wonder they now and then become "giant cells—gigantic cells," and practically inflammation seems to be a struggle between irritant bodies and white blood corpuscles.

Fourthly, I would name the "processes of disease" associated with the condition of "fever" of which Dr. D. MacAlister, of Cambridge, and Drs. Maclagan and Ord, of London, are the most recent exponents in continuation of the expositions of Parkes, Liebermeister, Burdon Sanderson, von Pettenkofer, and Ringer. A rise in the temperature of the body is an essential factor in the condition of fever with which many others are combined. The increase of temperature being measurable, clinical thermometers have come into general use to determine the existence or the absence of this factor of the febrile state. Up to 1864, the thermometry of disease had no home in England. Up to that period we look in vain for records of temperature in the clinical history of cases of febrile diseases published in our medical journals. It was not till 1865 that the temperature of the body in disease began to excite much attention in the metropolitan hospitals.[17] It is, therefore, very gratifying to me to find that since the time when the subject was first expounded in any English textbook on medicine in 1863, the importance of the thermometer in the diagnosis, prognosis, and treatment of disease has become more and more apparent, and the use of the instrument more and more universal. We have ample evidence of this in the numerous contributions to the literature of the subject during the past twenty-three years in the pages of our medical journals, and in separately published monographs. Hence the thermometer is now as much a necessity as the stethoscope; but what it tells us is not always easy to interpret.

In 1863, the first attempt in this country was made to bring the subject of the thermometry of disease to the notice of the profession in a systematic treatise,[18] and so to give thermometric observation the place it ought to hold as an aid to the study of disease. In that year and in that work, "diagrams illustrative of the typical ranges of temperature in the acute specific and in other febrile diseases were given for the first time in a textbook." The author of that work was induced to do so from a belief in the great practical importance of the subject, and with the hope that it would lead those who had opportunities to add to our knowledge of febrile diseases in this direction.

The first registering clinical thermometers for general use in this country were made by the veteran philosophical instrument maker, Mr. Casella, under my directions. But in their first large size they were soon found to be too cumbrous for general use, hence the thermometer was in danger of remaining a stranger in the practice of our art. But the great advantages to diagnosis and treatment, both direct and indirect, which were demonstrated to follow from an accurate register of temperature in disease, and the expressed wants of many men in large practice very soon brought about a manufacture of accurate clinical thermometers sufficiently small to be carried in the waistcoat pocket. For this the profession is mainly indebted to the representations of Dr. Clifford Allbutt, of Leeds, so that Harvey and Reynolds of that town, Casella and others in London and elsewhere, now vie with each other in producing neat and efficient clinical thermometers.

It is not to be inferred from these statements that during the past twenty-seven years thermometry has been for the first time studied in connection with disease. There is, indeed, no better example of the truth "that the success of a discovery depends more upon the time of its appearance" than the value of the thermometer in the diagnosis of disease. In very early times it was known that those suffering from various diseases often presented marked changes of temperature. But this knowledge was never formulated, nor was its full meaning perceived until within the past thirty years. Many interesting thermometrical measurements were made by Sanctorius, as long ago as 1638; also by Boerhaave and Van Swieten, and by De Haen about 130 years ago; and, in more recent times, by John Hunter, Robert Currie, Benjamin Brodie, and others. There appeared indeed to be no reason why the prosecution of such researches might not then have continued to advance. But the period was not ripe for the work. Physics had not supplied instruments of the requisite precision and delicacy to be efficient. No rational idea of the essential meaning of the changes of temperature in disease could be entertained until the more general laws of heat were known, and until it was established that the human body is at one in its movements with the forces external to it, and until the laws of the generation of heat in the body, and its co-relation with the vital and all the other forces, were discovered and confirmed. It is this solidarity between the vast onward movement of modern medicine and that of the other sciences which has made, and is continuing to make, our science so seductive and inspiring a study when pursued for its own sake; and hence it is always able to draw some of the ablest men of the time into its ranks, with a highly cultivated education and training in the collateral sciences (Clifford Allbutt).

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[17] *Lancet*, December 9th, 1865, p. 647.

[18] *The Science and Practice of Medicine*. By William Aitken, M.D., F.R.S., Professor of Pathology, Army Medical School, Netley.

It was in 1851 that Traube, as a physiologist and physician, published in Germany the earliest systematised thermometrical observations of febrile diseases.

In this country the late Dr. Parkes was amongst the first to use the thermometer as a means of clinical instruction at University College Hospital. So early as 1853 he had made both thermometrical observations and urine analyses in fever, which so far confirmed those of German observers. In his Goulstonian Lectures on Fever, published in 1855, he then for the first time insisted upon and demonstrated the uses of the thermometer in clinical work. We point with pride to these researches, for by his investigations into the tissue-changes in febrile diseases he largely contributed to the extent and accuracy of modern doctrines. There were, indeed, few subjects in practical medicine which during his busy life he did not touch as a teacher and as an experimentalist; and there was no subject he touched which he did not elevate and adorn. His mind, graced by the possession of the imaginative faculty, tempered by culture and chastened by natural refinement, shines forth in its greatest perfection in these classic lectures, pregnant with suggestions for work still to be accomplished. Adopting the opinions of Virchow, Parkes showed how numerous febrile disorders are attended by variations of temperature, having a very intimate relation to the whole bodily processes. He showed, by original clinical observations, that in all fevers there is increased metamorphosis of tissue; and that this metabolism is effected through the agency of certain parts of the nervous system, and how increase of temperature is the most constant objective sign of the existence of fever.

In all respects medical thermometry during the past thirty years has been shown to be of increasing significance and importance. It gives us the most intimate knowledge we can have of the variations of functional balance. It is a most subtle indicator of disease; a most accurate measurer of conditions affecting the body whether in health or disease; but it cannot tell us whether the increased temperature is due to an increased production of heat, or to a diminished loss, or to both. Cotemporaneous with Dr. Parkes in this country, I would mention the name of Mr. (now Sir) John Simon, who in his erudite reports to the Privy Council on public health contributed largely to the development of the value of thermometry in disease. Thirty years ago, German students and physicians had been familiar with the uses of the thermometer; but with the exception of Mr. Simon and the late Dr. Parkes, and the pupils he taught in University College Hospital (and perhaps a few other distinguished hospital physicians), the usefulness of the thermometer in recognising febrile diseases had not been appreciated in the medical schools of this country. Even now, however, the thermometric observation of diseases is but yet a recent industry. If not still in its infancy, it is merely in its youth. Many interesting monographs have been written on it, while many physicians and general practitioners in the larger towns all over the world are at daily work with the thermometer, stimulated by the results set forth in the works to which I have referred. But as yet only one treatise has been published which deals adequately with the whole subject, namely, that of the late Dr. von C. A. Wunderlich, of Leipzig, published in 1868, twenty years ago. "It is a work which shows such perseverance and thoroughness, such caution and insight, such wide and minute learning and experience, that it has not only established this branch of investigation for the first time upon a deep and lasting basis, but it has built up the edifice to a great extent; and points out with clearness the directions in which future labour must be applied" (Dr. C. Allbutt).

One important distinction has gradually become clear from the use of the thermometer, namely, those high abnormal temperatures due to the specific fevers, as distinguished from those high temperatures due to lesions of the nerve centres. This distinction is the gradual outcome of the accumulation of facts, and the collection of truths inferred from facts by successive observers in recent years. In illustration of this we have (1) Sir Benjamin Brodie's case, in which inordinate elevation of temperature occurred upon a crushing injury to the cervical portion of the spinal cord. (2) There is the case which Mr. J. W. Teale, of Scarborough, communicated to the Clinical Society of London, in February, 1875, in which a temperature ranging from 108° to 122° F. had been maintained for a period of nearly nine weeks. The patient, thrown from horseback, had serious injuries to the spine and ribs. Three years and nine months after this injury, Dr. Teale informed me that the patient continued to suffer great pain in the back at times, when the temperature rises somewhat sharply. (3) Similar cases described by Dr. Donkin. (4) Those experiments on living animals in which different regions of the spinal cord have been accurately divided, causing increase of temperature. The most recent are those done by Dr. H. C. Wood, whose conclusions have been published by the Smithsonian Institution of New York. He found that sections of the nervous tract at the junction of the pons and medulla, by which the vaso-motor centre is unaffected, lead to a large increase of heat production, which is independent of any change in the blood pressure or heart beats. But Dr. D. MacAlister has greatly extended our accurate knowledge of heat production, and the outcome of recent experiment is that fever consists in a greatly increased tissue metabolism, with simultaneous increase of temperature; the mechanism regulating the balance, the formation and the expenditure of heat being disturbed. The body is thereby incapacitated for doing mechanical work, so that the amount of potential energy transformed is almost all converted into heat. Hence the consuming or wasting character of fever. It has been shown that the production of heat is most abundant where the metabolic changes are most active, namely, in the voluntary muscles, and in the glands in part. Muscles are shown to have a double function, motional and "thermogenic," and in abnormal states the thermogenic function may become obvious withous the contractile function being exercised. The definite result of experiment further shows that a special nervous mechanism, including one or more nerve-centres in the cerebrum, control the "thermogenic" function in muscle. All agree in placing the chief heat centre above the pons—a localisation of fundamental importance, since it excludes any implication of the chief vasomotor centre in the upper part of the medulla. But precise localisation is not yet fixed.

The registration of local temperatures has more recently attracted attention, and with successful, because definite, results. The precise locality of cerebral lesions have been also thus determined by Broca and others, so that a positive value for local thermometry may now be accepted as an aid in making regional diagnosis.

Fifthly, I would mention the combination of many factors concerned with the process of local death, necrosis, and gangrene of tissues and parts. This is of great importance in connection with the occurrence of microbes in specific diseases.

Sixthly, the nature and extent of "the degenerative processes." Degeneration is a term unknown in our medical textbooks up till 1860. The microscope has since enabled us to discriminate various forms of degeneration, and to recognise especially (1) those which are simply the result of age, "from the cessation of the influence of that formative force which first builds up, then maintains existence, and then finally dies out, leaving behind a tissue or a structure of an organ worn out, effete, and useless." The general diffusion of such degenerations is characteristic of advancing age. They are of the nature of decay and death; so that parts of us are dying while we ourselves continue to live. Hence the name of "necrobiosis" which has been applied to them, because degeneration and death seem to be naturally brought about towards the close of our existence. In this respect it has been truly said that "as we begin to live, we begin to die." (2) The second great class of degenerations are those which are the result of disease. They are the slow but certain result of some excessively slight but continuous failure of some process in nutrition.

We are now able daily to recognise how fibroid, fatty, pigmentary, calcareous, atheromatous, and molecular wastings and degenerations, especially of muscular fibres, large and small blood vessels, of gland cells, of mucous membranes, of nerves and nerve centres come to complicate the more acute maladies, and largely increase their mortality both in medical and in surgical practice. Hence the probability of degenerations being present, not only in aged but in middle-aged patients, is at once an embarrassment in prognosis, and the existence of degeneration will oftentimes account not only for failure in treatment but for sudden death.

The mere separation of these degenerations from the substantive diseases which has been effected during the past twenty-eight years is regarded as one of the greatest advances in modern medicine. Such is the opinion of one of the most eminent physicians of our day, Sir William Jenner; and the recognition of them has very much modified our practice and experience in recent years, especially as regards the diagnosis and treatment of degenerative heart diseases, and certain forms of apoplexy.[19]

It must be admitted, however, that these degenerations are still diagnosed during life with great difficulty, except where the kidney or muscular substance of the heart is their seat; while the slow degenerations of the mucous membrane of the alimentary canal, and those of the various regions of the spinal cord, and nerve centres in the brain are still amongst the most puzzling of maladies. After death they can only be recognised in the affected parts by using the higher powers of the microscope. "In the means of detecting the presence and estimating the amount of these degenerations we have still much to learn; and a faithful analysis of the circumstances under which they have arisen, and a recognition of how they are to be avoided would confer a great benefit on the human race" (Parkes).

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[19] *The Practical Medicine of To-day*, by Sir William Jenner.

Seventhly, I would mention the processes connected with the formation of new growths, the processes of cell-multiplication, or cell-proliferation, the formation of tumours and their relation to embryology, their identification as "innocent" or "malignant," and the infective nature of malignant growths.

It was as a physiologist that Cohnheim, in his classical *Lectures on Pathology*, insisted on a wider conception of the subject of cell-formation and growth than had hitherto been given to these topics. A too exclusive, or rather an undue, importance had been attached to the "mere form of cells" and to mere alterations of structure. The tubercle corpuscle of Lebert, the cancer cell, the typhus cell, the giant cell, the microcyte, all have had their day as absolute criteria of particular diseases; and in all our microscopic work we have been too apt to bestow undue attention to visible changes apart from the more important vital processes which underlie these changes. But a reaction has set in, and it has now become the aim of pathologists to discover what structure, if any, is always associated with certain living conditions—with, for example, malignant properties. The researches in this direction during the past thirty years may now be summed up in the following results:[20]

1. There is no kind of structure absolutely characteristic of malignant growths.
2. It may be broadly stated, nevertheless, that malignant growths are nearly always heterologous or atypical in structure, and that typical or simple growths having such properties are quite exceptional, the only simple tumour at all frequently malignant being "lymphoma."
3. The great majority of malignant growths fall under one of two heads, either "sarcoma" on the one hand, or "carcinoma" on the other; the latter having, as a rule, more definitely malignant properties than the former.

But these results do not give a sufficient nor a convenient basis for practical rules of diagnosis. And here again physiology comes to our aid. As physiologists we argue from structure to properties by adopting the biological method in natural history. This method consists in arranging all morbid growths for purposes of classification and diagnosis according to their structure solely, and not according to properties, in the first instance. Having thus determined the systematic position and name of a growth, we have all the existing recorded experience respecting its properties and character, an experience now so large, that there is usually no difficulty in predicting from the growth what is likely to be its future history, its course, and its effect on the organism, except in the improbable event of our having to deal with an entirely new kind of tumour. This is exactly what we do in botany and in zoology. When we have determined the name of a plant or of an animal, we can then learn all that is known of its habits and properties, but we do not find it necessary to classify plants according as they are useful, poisonous, or harmless, and animals as rapacious, or innocent and the like. Hence a classification of tumours on structural grounds is that which has at present most practical value as well as the highest scientific completeness.[21]

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[20] *Manual of General Pathology*, p. 256, by Joseph Frank Payne, M.D.Oxon., F.R.C.P.

This, then, being our present position as to tumour growths, we must try and not lose sight of the spark in the flame it has served to kindle, as is usually the case. While Johannes Müller was the first to systematise pathological histology as applied to tumours, and was followed in the same direction by Henle, Gluge, and Vogel; it was Rudoph Virchow who showed how cell changes are concerned in all morbid growths, and in a vast number of diseases; and how in cell systems and in cell territories disease processes may be often localised. The "cellular pathology" of Virchow was at the time, and still is, the most important exposition of the elemental side of pathology, but it has never entirely displaced what may be called the "central," or vascular theory,[22] and of late years the "cellular pathology," while it has undergone serious curtailment in some directions, especially in its application to the phenomena of inflammation, and in respect to the importance of the connective tissue in relation to disease, it has expanded in other directions, and has tended much to widen the area of practical pathology. But apart from its great value as a study in histology and physiology, Virchow's great work did an incalculable service in sweeping away fallacies that still lingered, in compelling attention to the most minute changes which lie at the root of disease, and in showing how in these minute changes are to be sought both the evidence and explanation of functional disorder.[23] Hence the doctrine is every day becoming more securely established—that there can be no alteration of function without some material change. Virchow made a study of the living cell as distinguished from dead tissue—of the cell endowed with vitality and with functions, governed by laws of existence, and capable of self-multiplication and propagation, and the arrangement of them in territories and organic systems. He studied the cell as the living agent in the production of disease, or in the arrest or perversion of its action by disease-producing causes.

It is, indeed, the great merit of Virchow's work that, passing by the mere study of structure, he endeavoured to show how the morbid changes came to be developed, what were their bearings to living action, and what their relations to the normal processes of evolution, development, and growth.

At this point the present era of modern pathology may be said to have begun.

In the first thirty years of the century we had the renewed study of general anatomy giving a new impulse to the study of mere morbid anatomy, both in relation to normal anatomy and to clinical medicine.

During the next thirty years we had the more general application of morbid anatomy to clinical medicine as an expounder of the phenomena of disease. At the same time there came a fuller knowledge of the structure and functions of the several organs, and the more elaborate working out of detached portions of normal and pathological histology, rendered possible by the great improvements in the manufacture of microscopes and their lenses.

But when, in 1860, Virchow's work became more fully known through its English translation, that event may be looked upon as the culminating point of the period, the commencement of the present era of progress in the science of pathology—a progress which has made gigantic strides, advancing by leaps and bounds throughout the past twenty-eight years.

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[21] Payne, *loc. cit.*, p. 257.
[22] Editor, JOURNAL, October 23rd, 1880, vol. ii, p. 655.
[23] Professor W. S. Greenfield, JOURNAL 1881 vol. ii, p. 695.

"During the past ten or twelve years also, and especially during the last three or four, still more important advances have been made as to the minute structure of the cell and the functions which it performs in its reproductive processes. The mobile molecules of which it is composed are constantly changing—giving to, and taking from, the outer world—manifesting by their special action on polarised light, and by their reducing influence on the salts of silver, the intense molecular activity that undoubtedly prevails in the inner world of living matter."[24]

Further, the minute structures that since 1882 have been shown to characterise the nuclei of cells have probably a definite physiological purpose (Strasburger and Flemming). The nucleus is not the simple structure that has been hitherto supposed. The chemical nature of nuclear matter has still further opened up to us a new world of real phenomena; and molecular science sets us face to face with physiological (and pathological) theories, and forbids alike the physiologist (and the pathologist) from imagining that mere structural details of infinitely small dimensions can furnish an explanation of the infinite variety which exists in the properties and functions of the most minute organisms.[25]

Eighthly, processes immediately connected with changes in the blood, the nature of "leukæmia," and of the crystals found in leukæmic blood by Professor Charcot must be noted.

Ninth and lastly, I would mention those "processes of disease" associated with minute microscopic parasitism, animal and vegetable, which are so extensive that their recognition (if fully established) will revolutionise whole fields of pathology.

In these investigations the names of Rayer, Davaine, Pollender, De Bary, Flügge, Klein and Gibbes, Baumgarten, Eisenberg, Greenfield, Crookshank, Woodhead, Pasteur, Friedlander, Koch, Watson Cheyne, Cohen and Zopf, Hüppe, Weigert, Klebs, Gaffky, Obermeier, Hüber and Becker, Burdon Sanderson, and many others will be associated for all time—investigations which have greatly enlarged our knowledge of minute structural changes, necessitating still more extended inquiry and study alike of morbid anatomy and chemical and biological changes, so that new facts and new discoveries are daily being added to our already overwhelming stores. Here the need for generalisation is urgent, so that laws may be evolved which will bind together the immense accumulation of such facts as may be substantiated.

As to Causes of Disease.—1. We have undoubtedly learned much from a knowledge of the action of poisons which are known and can be experimented with. We have thus learned to appreciate the action of "specific poisons," as causes of certain diseases. 2. We have learned to appreciate the nature and action of ferments, also of animal and vegetable poisons as causes of disease; of substances formed by living animals and plants, often the products of special glands and having physiological uses, all of which may become injurious or poisonous. 3. We have learned to appreciate the nature of septic and cadaveric poisoning, of fæcal poisoning, and the effects of decomposition products in the living body, the causes of cadaveric, fæcal and septic decomposition—the formation of the ptomaines or cadaveric alkaloids and of the leucomaines in the living.[26] 4. We have learned to appreciate the influence of "specific morbid poisons," so called because they are believed to be capable of producing each one special disease and that only. The question of a "living contagion," is at present only represented by that analogy which subsists between a possible contagium and the growth of some living thing. The actual contagium is in the case of most specific diseases still unknown.

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[24] *The Modern Cell Theory*, etc., by J. Gray McKendrick, M.D., LL.D., F.R.S., *Proceedings of Physiological Society of Glasgow*, 1888.

[25] Art. "Atom," in the *Encyclopædia Britannica*, by Professor Clark Maxwell.

While we thus far recognise physiology and pathology as the basis of the science of medicine, the physiologists (through biology) have hitherto immeasurably outstripped the pathologists in the comprehensiveness of their views, and therefore in the value of their results. For this reason we are compelled to recognise a pathology which may be described as indirect, or as only inferentially based on anatomy and physiology, Dr. Hughlings Jackson is the able exponent of this pathology. As a physiologist, he has expounded (as far as anatomical knowledge permits) the pathology of epileptiform affections. With the help of Hitzig and Ferrier's experiments, epileptiform seizures are shown to be more or less localised; and to be only a great excess of the normal physiological action, a great exaggeration of the liberation of energy, by some part of the nervous system. We thereby infer that a group of nerve cells has become permanently abnormal, and highly unstable and uncertain in action. But this anatomical knowledge is only vaguely inferential; and while we recognise the physiological process, physiology has not yet sufficiently opened the gateway of knowledge to enable us to find out the pathology of this terrible disease, and to ascertain "by what abnormality of nutrition the local hyperphysiological condition is produced," or in what tissue of the nerve organ does the abnormal change begin. And, indeed, in most diseases of the nervous system our knowledge of their pathology is only indirect and inferential. We do not know that the essential elements—nerve cells and fibres—go wrong primarily, but that they suffer indirectly. And nearly all diseases of the nervous system, of which there is a known morbid anatomy, are diseases beginning in the subordinate elements. The nervous tissues are innocent, and suffer only as a secondary result. For example, the commonest nervous affection is primarily an affair of the arteries. Hemiplegia in the majority of cases is due to blocking up of a diseased artery, or to a rupture of one, and the nerve tissue suffers only as a consequence. It is locally starved, because its blood supply is cut off, and to find out the pathology of the arterial lesion, we must make a study of cardiac, arterial and renal diseases, as well as of syphilis, gout, and rheumatism, and so we learn, indirectly, the pathology of nervous diseases.

Dr. Hughlings Jackson continues to point out that the syphilitic affections of the nervous system are the most important clinical groups of such cases. Anatomically, it is certain that the syphilitic lesion begins primarily in subordinate tissues of the nervous system, unless where a definite nerve trunk is directly the seat of the lesion, otherwise the process is an indirect one. Syphilitic hemiplegia, no doubt, depends on "local softening of the brain," and indirectly on the syphilis. The order of events is, that the man gets (1) a chancre and subsequent secondary symptoms; (2) months or it may be years later when apparently well (except perhaps for headache), some of his cerebral arteries become syphilitically diseased, and one unfortunate day a branch gets blocked up and hemiplegia results. For this apparently simple accident, there has been a long, slow, insidious degeneration of the vessel going on. The syphilitic degeneration is slow, but the thrombosis is rapid, and the brain softening follows as an indirect result of the syphilis.

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[26] *On the Animal Alkaloids; the Ptomaines, and Leucomaines, and Extractives in their Pathological Relations*, by Sir William Aitken, Knt., M.D., F.R.S.; also *A Treatise on the Animal Alkaloids, Cadaveric and Vital*, by A. M. Brown, M.D.

There is also another kind of syphilitic hemiplegia, due to the formation of a cortical gumma; and one day the patient has a convulsion (often beginning unilaterally), and afterwards he becomes temporarily hemiplegic. The "disease process" here leading up to the hemiplegia is a very *indirect* one. The nerve cells round the gumma are irritated into exaggerated nerve discharges, and the pathological stages are: (1) the syphilitic infection; (2) formation of a gumma; (3) induction of instability of function in the nerve cells, exactly as by a glioma, or perhaps by some encephalitis; (4) sudden excessive discharges of motor energy in the form of epileptiform convulsions, and (5) consequent hemiplegia. The physiological gate is not yet opened wide enough for us to appreciate the pathology of chorea, epilepsy, insanity, neuralgia, hydrophobia, or tetanus.

We have now come to a point at which it is obvious that ordinary human physiology is not in a position to elucidate all pathology. We find that there is undoubtedly a large class of diseases for which we have not yet found a link to connect them with mere perturbations of normal physiological life; and that a great deal of pathology appears to be quite different in kind from any physiology known to us. What, for example, are the physiological analogies of the "constitutional" and "infective" diseases? For it has hitherto been held that the specific infective diseases cannot be included in the physiological scheme of diseases which I have thus far attempted to illustrate. These constitutional and infective diseases constitute so large a portion of medical ailments that diseases whose pathology is explicable, on strictly physiological principles, are rather the exception than the rule. There would seem to be no place in a physiological pathology for the long list of specific infective diseases, such as cholera, yellow fever, plague, typhus, enteric fever, small-pox, leprosy, syphilis, cancer, consumption. Hence these diseases still constitute the real difficulties of pathological science.

It seems that the logical outcome of the position arrived at is "that we can conceive of any one of the so-called specific diseases arising *de novo*, as must certainly have happened at some period of the world's history for the first time; and that, having so arisen, the disease subsequently acquired an autonomous or independent existence, and became capable of transmitting its life apparently only by infection."[27]

Dr. Charles Creighton[28] in his interesting address to the Association made an important contribution to pathology from this standpoint in his account of what he believes to be the *de novo* origin of some specific diseases.[29] He attempted to show, with much success, that the acute specific diseases are, in their origin, to be explained on biological laws. He showed that in these diseases we have what he describes as a "pre-autonomous" stage, and afterwards an "autonomous" stage. The pre-autonomous stage of disease is that stage or state in which there is merely a perturbation of the physiological processes. When, however, the disease has become established in all its clinical features it has passed into the autonomous or independent stage, when the functional disease acquires individuality, and by-and-bye the power of infection, it thereby asserts its independence, its autonomy, in working out this formula he endeavours to find some relation between common aberrations of structure and function and the specific infections, or a relation between disordered states of the body and the self-existent species of diseases. Is it possible, for example, in the case of cancer and tuberculosis (consumption) to show that these malignant and wasting infections have arisen out of common disturbances of the physiological life? Whether we do not find, in the case of tuberculosis, a pre-tubercular stage (an old belief) by small beginnings in certain disturbances of nutrition which devitalise the tissues? And whether we do not also find a pre-cancerous stage of cancer in certain irregularities of the apparatus and process of secretion? These beginnings would correspond to the pre-autonomous stages of these diseases; while the autonomous life of each of them asserts its semi-independent existence through the quality of infectiveness. Both of them are at once constitutional, hereditary, infective, and perhaps contagious. "The cancerous element comes in usually after a particular time of life, characterised by the implication of other tissues than the glandular or secreting structure whose irregularities were the exciting cause. Epithelial cells that have not been used for secretion can become mischievous as infecting cells; and if we examine the affected region we shall find an epithelial-like kind of structure springing from the tissues around where there is no epithelium naturally; a little later the same epithelial pattern is, as it were, carried out in the lymphatic glands, or in the liver, or in the deeper layers of the skin, or even in still more unexpected places. The pattern of this widely distributed structure is always the same in a given case, and there is always something in it which reminds us of the primary seat of glandular disturbance. An intelligible disorder of structure and function not without its close analogies in physiology (animal and vegetable) has thus acquired a kind of individuality or independence and a power to reproduce itself throughout the body. In other words, by its infectiveness it has become a ravaging cancer."[30]

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[27] Millican, *Evolution in Disease*, p. 46.

[28] On the Autonomous Life of the Specific Infections, JOURNAL, August 4th, 1883.

[29] Hirsch *On Geographical and Historical Pathology*, vol. i.

The disease may thus be traced along the track of physiological perturbations for a certain distance, after which it assumes a semi-independent life, and becomes an *imperium in imperio*—a power inseparable from the general life of the body, but in the end sure to gain the mastery. In vegetable physiology we have this analogy: "that when the corm of a crocus forms the bud which is to be the bulb of next year there is the gradual differentiation of the being until it becomes an *imperium in imperio* and finally an *imperium* in itself. Does not the new bud act the part of a cancer in reference to the old, eating out its life and substance, and leaving it a dried-up husk? Then, again, has not the bud of this year the germ within it of the bud of next year? And we cannot tell how many potential existences are thus wrapped up inside of one another. There is no germ or sperm action here. (A. W. Wallace, of Parsonstown.)

In animal physiology the effects of cross-breeding furnish remarkable analogies.[31] We know that the contact of the spermatic fluid will set an action agoing in the female of some animals which results in the production of myriads of proliferating cells. If these were retained in the body, instead of being extruded as ova, would it not be a case of "exogenous contagium;" and to carry out the parallel between this and the acute specific diseases, "the male which produces the infective (spermatic) germ is incapable of producing the proliferating cells which are the analogues of the germs of the infective diseases. Again, some plants grow either by spores or by fission. May not then a specific disease take its origin and be propagated by the distribution of the germs which have been formed during its progress? May not this explain the origin of typhoid, scarlet fever, etc., out of the same foul drain? May not the infecting germ originate a different kind of proliferating cells, according to the reaction with which it comes into contact, as the same semen may produce either a horse or a mule.[32]

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[30] Address in Pathology, by Charles Creighton, M.D., JOURNAL, vol. ii, August 4th, 1883, p. 219.

[31] Consult Harvey, on *The Identity of the Bud and the Seed*, Nisbet and Co., 1887, p. 61.

To find the proper biological analogies for the infective disease processes is the task of modern pathology.[33] Hitherto we have been too much given to study cases as to how near their symptoms approach to certain clinical standards which we consider typical, as laid down in books, and not as they merely show departures from healthy types, that is, from those normal physiological processes which maintain the state of health.[34]. Working in this comparatively narrow groove we have become oblivious to a great mass of facts, increasing from day to day, which cannot be explained on the older theories of pathology; but much evidence is accumulating in favour of a theory of progressive evolution, as sufficient to explain not only the origin of many forms of "constitutional" or "inbred" diseases, but also the progressive development of specific fevers like enteric fever, scarlet fever, and diphtheria, from simple cases more or less anomalous, and obviously departures, in the first instance, from the usual types of these diseases, gradually acquiring specific infectiousness and independence of existence as the cases multiply.

I have had myself experience (and perhaps many in this room are prepared from experience to admit) of sore throats commencing in more or less acute tonsillitis, due apparently to indifferent causes, but gradually becoming more and more severe as case followed upon case, until (as if by progressive development) they eventually culminated in scarlet fever or in diphtheria, with its unmistakable sequelæ of paralysis. Such cases thus acquire (by a process of evolution through several individuals) their typical infectiveness, each new case furnishing its quota of pernicious material to its surroundings, and thereby adding to the virulence and amount of concurrent factors, and so eventually setting up the independent infective disease.[35]

Similarly, cases of diphtheria have been shown by Dr. Thorne[36] and others to be evolved from cases of membranous croup, inasmuch as it was observed in several outbreaks of diphtheria that while the earlier deaths were due to membranous croup, the later ones were due to malignant diphtheria. Over a large area there would be a great tendency to sore throat; then groups of cases would occur here and there in which the disease became decidedly infective, and at last, in a single village in the area, an outbreak of diphtheria would occur in its most malignant and fatal form.[37]

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[32] A. W. Wallace, M.D., of Parsonstown, JOURNAL, August 18th, 1883, p. 361.

[33] Dr. Creighton, on the Autonomous Life of the Septic Infection, JOURNAL, August, 1883.

[34] Hughlings Jackson, *loc. cit.*

[35] See "An Address on the Etiology of Diphtheria," by Edgar G. Barnes, M.D., London, of Rye, Suffolk, in the JOURNAL of July 28th, 1888, p. 173.

[36] Report of Medical Officers of Health.

[37] Millican, *loc. cit.*, p. 80.

But I could wish no better example, because without bias, as to the question of the gradual evolution of zymotic disease than that furnished by the Director-General of the Army Medical Department of the War Office, Sir Thomas Crawford, at p. 4 of the very comprehensive memoranda which he recently issued for the guidance of the officers of the medical staff of the Suakim expeditionary force. There it is written: "The events making up the medical history of an army in the field develop themselves with a regularity that is almost monotonous. Looseness of the bowels, under the name of camp diarrhœa, begins to be common almost as soon as the army takes the field. This is in a large number of cases compatible with apparently good health, and is doubtless attributable to the changed condition of life. Soon cases of fever appear, some of very brief duration, which are classified as heat fever, and some are attended with diarrhœa, marking the commencement of enteric fever in the force. The development of this disease and the proportions it will assume will be merely a question of time and circumstances. The disease embraces every variety, from the mildest to the severest types, from the so-called ambulant to the most fatal forms. The instances in which this fever occurs as a relapsing typhoid properly so-called, with an invasion fever period, followed by one or more febrile recurrences in which all the characteristic phenomena are repeated with intervals of apyrexia between them, are also not uncommon. The disease occasionally runs so mild a course as to resemble a febrile dyspepsia, and then the thermometry of the fever either fails to be recognised at all, or at any rate fails to be recorded with any degree of accuracy."

Again, I think it will be admitted that no broad nor defined lines can be drawn between the severest cases of cholera and those slighter and generally curable cases which are seen during the prevalence of an epidemic, or which occur as sporadic cases during its intervals. An attentive observer may trace up every grade from the merest cholerine to the terrible disease which kills inevitably in a few hours. The cases may, in fact, be seen to pass into each other, and the one may seem to induce the other, so that an alliance is implied, at least, in such a possibility. Abrupt lines of demarcation between such allied affections have no existence in Nature.[38] So, too, erysipelas is seen to be interchangeable in lying-in hospitals with puerperal fever (Playfair); also that diphtheria and puerperal septicæmia are one and the same (Hicks). Moreover, we have seen that the association of diphtheria and scarlet fever is not infrequent; and on the testimony of so competent and experienced a physician as Dr. Broadbent, the approach of diphtheria may be absolutely independent of any pre-existing cause; while so distinguished a physician as Sir William Gull has stated his belief that diphtheria "may commence locally, forming a poison which will propagate itself."[39]

The recorded irregularities from the artificial clinical types of disease are now so numerous that they form a very large class, still standing alone—so large a class, indeed, that, comparatively, the so-called typical cases of specific diseases become an insignificant minority. Practically, for example, it has not been found possible to classify all the fever cases under the definite types described in books. Cases of an anomalous or mixed nature do constantly occur, concerning which a distinctive diagnosis cannot be made. While certain forms of continued fever are capable of being recognised as described, there can be no doubt that cases of fever do occur all over the world, which run a continuous course;

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[38] Dr. E. A. Parkes, *On Cholera*, p. 5.

[39] JOURNAL, May 3rd, 1879, p. 666.

but, having no other specific characters, and which in many respects do not seem quite the same as those with which we are familiar, and which can at once be clinically recognised. For example, the late Dr. Murchison records[40] that he had to leave out of consideration about 200 anomalous or doubtful cases, which he could not classify as either typhus or enteric fever. So, also, our distinguished president, Professor W. T. Gairdner has stated that from 1853 to 1862 the cases of fever in the Edinburgh Royal Infirmary under his notice, included "numerous anomalous fevers, which have quite overborne the numbers of genuine typhus and enteric fever together."[41]

On the other hand, with regard to the "constitutional diseases," their pathology finds a direct explanation upon purely biological principles, in which heredity plays a prominent part—a property of parental origin, representing the innate tendency which each organism possesses to reproduce its like, while another influence exists in the action of the environment upon nascent organisms. The three great principles which regulate variation, namely (1) the tendency of offspring to differ slightly from their parents; (2) inheritance, or the tendency of offspring to resemble their parents; and (3) atavism, or the tendency of offspring to resemble remote ancestors, are sufficient to account for the remarkable diversity which has been brought about by the steady accumulation of innumerable slight variations alike in health and in disease. With regard to diseases, there is ample evidence to show that certain variations are more apt to be inherited than others; for example, skin affections, affections of the nervous system, and of the generative organs. Also that modifications result from the action of unusual agencies on the embryo, and that processes of repair take place the more readily the younger the age of the subject.

So also Dr. Wilks has written in one of his thoughtful addresses to the Association,[42] that "hereditary tendencies have much to do with the physical and mental characters of individuals; that the temperaments and idsosyncrasies so evolved are most important factors in the production of our ailments, and that our surroundings (environment) are in themselves sufficient to produce active disease. There are, for example, a number of conditions which tend to the development and prevalence of the gouty constitution in England which may be carried through several generations, while the same conditions operating on a person already predisposed may actually induce an acute attack in him. Many diseases thus come about through the deleterious operations of our ordinary surroundings, both in the air we breathe and in the food we eat, rather than from any single and well-defined specific cause. Nearly all such diseases are slow in their origin and progress, and as Hippocrates wrote, they 'do not fall upon men instantaneously, but being collected by slow degrees, they explode with accumulated force;'" and it must still be the aim of the physician to seek the causes of much disease in our ordinary surroundings, and in the constitutional tendencies transmitted to us, and to try to remove them.

Sir Andrew Clark,[43] the President of the London College of Physicians, has very clearly summed up the pathology of these diseases in these words: "Do we not find that, for the most part, such diseases are of very gradual evolution, the essential outcome of continued violation (consciously or unconsciously) of physiological laws, as they exist for the race, or as they are conditioned by the peculiarities of the individual; that these violations are not exceptional and gross, but daily and minute, and that their specific effects, infinitesimal from day to day, become visible only after long periods of time, and so escape recognition except by those who are trained to discern the causal connection of subtle things?" Such an evolution is thus apt to be unnoticed from its slowness; but it is just these minute and almost inappreciable conditions of daily life which practically make or unmake health. Slight variations, moreover, are also being introduced in Nature with every successive generation of existences. Many of these variations are transmitted to the generations which follow, and therefore in the course of time, from any one parent stock would descend a great variety of kinds, and with them we should expect to find variations in diseases—constitutional and hereditary, and perhaps also infective. Hence it may be fairly inferred that the long-continued influence through many generations and ages of time of hereditary influences, and of unsuitable but inevitable environments may establish new diseases of constitutional or autochthonous production, and if not absolutely new diseases, at any rate diseases of such variable chronic types as are daily met with and classed as general or constitutional ailments. The effects of physiological forces acting under unphysiological conditions constituting the essential and true disease.

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[40] *Transactions of Royal Medical and Chirurgical Society*, vol. 41.

[41] Dr. W. T. Gairdner, *Clinical Medicine*, 1862, p. 154.

[42] JOURNAL, vol. ii, 1885, p. 196.

[43] *Transactions of the Clinical Society*, vol. xvi, p. 57.

So far, therefore, as the doctrine of evolution in biology has assumed a position and acquired an importance ever since 1859 which it had not possessed before, it is, I believe, especially capable of illustrating the pathology of constitutional diseases from the biological view here indicated.

From this point of view the constitutional diseases may be regarded as "sports" or "variations" from the normal line of health. Evolution may thus not only explain their origin, but may account for the persistence of some forms of diseases unchanged through long epochs of time, while others undergo comparatively rapid metamorphoses. The causes and conditions of variations in constitutional diseases, as in biology, have yet to be thoroughly explored, and more extended inquiry may prove "that variability is definite, and is determined in certain directions rather than in others by conditions inherent in that which varies..........It is quite conceivable that every species of constitutional disease tends to produce varieties of a limited number and kind," and that the effect of some kind of "elective affinity" in the constitution of the race, or of the individual towards certain causal and concurrent factors of disease rather than to others would be "to favour the development of some of these, while it opposes the development of others along their predetermined lines of development."[44]

While these diseases appear to be developed under the influence of agents generated within the body itself, through the customary exercise of its functions in the daily course of nutrition, development, and growth, the original organisation of the body may be of such a kind that the continuous exercise of its functions, in place of preserving the system in a state of health, ultimately leads to the evolution of diseases of various kinds, which, from their mode of origin and development, have received the name of constitutional diseases.[45]

Altogether, therefore, it seems undeniable that the characters and variations of species and of constitutional diseases are due to the combined action of internal and external agencies, acting in a more or less direct, positive, and constructive manner, suggestive of an "intelligent purpose, which is, as it were, incarnate in the living world."

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[44] *Science, Culture, and other Essays*, T. H. Huxley, LL.D., F.R.S., 1881, p. 347.

[45] Aitken's *Science and Practice of Medicine*, various editions from second to seventh inclusive; also Dr. Farr in *Sixteenth Annual Report of the Registrar-General; Appendix*, 1856.

There can now be no doubt that changes of type alike in the inherited and in the so-called specific fevers do take place; "but we are prone to think too little of the variations—to regard them rather as unmeaning exceptions, or as the result of some unusual external conditions diverting diseases from their customary course. It will be better for us if we study in pathology, as in natural history, varieties as much as species, changes as well as more stable forms. It will then be impossible not to perceive, to reflect on, and to appreciate the pertinacious persistence of some forms amidst the vast mutations of others. Types of disease there are, the tenacity with which they are maintained—some even from prehistoric times—in all the variety of the conditions of our lives, is one of the most remarkable facts in all pathology. But even they are not unalterable. Types vary in diseases as they do in species; even in diseases which depend least upon external conditions, and most on the qualities which are transmitted by inheritance." These are the words of one of the greatest surgeons of modern times, and the most philosophical of pathologists—Sir James Paget—as to the value of recording "anomalous" cases of disease, and he proceeds to lay down rules for study especially applicable to them. "It would be of use if such cases were collected by the hundreds and thousands, and we ought not to set them aside with idle thoughts or words about 'curiosities' or 'chances.' Not one of them is without a meaning—not one but might be the beginning of excellent knowledge, could we but answer the question, 'Why is this?' Or, being so rare, 'How or why did this instance happen?'"

In his eloquent Bradshawe Lecture (1882) Sir James Paget further expresses his belief that there are rare cases, which are also cases of diseases lately new, and becoming more frequent, and which are mainly due to morbid conditions changing and combining in transmission from parents to offspring. Medical journals and Proceedings of Societies teem with records of such rare cases of diseases, some of which, although apparently common, differ in some feature from the usual type or standard of such common ailments; and hence they must rank amongst the "anomalous" cases of disease, to be considered as pathological "sports" from normal physiological states.

I would now quote the opinion of one not less eminent as a physician—the late Dr. Parkes—as to the value of recording "anomalous" cases of continued fevers and specific diseases. "It is these doubtful or anomalous cases," he says, which require careful and special methods of investigation. They are of the utmost importance to science, for more extended information regarding them will either connect them with forms of fever between which they seem to stand; or these "doubtful" cases will eventually separate themselves into distinct forms whose history is still unknown. Dr. Millican[46] has made a laudable attempt to classify these doubtful or anomalous cases.

These and such-like examples of the progressive development of disease from a simple ailment to a more complex case—from a comparatively benign and common inflammation to a malignant infective type—through a series of many cases, proceeding from a common origin—furnish cumulative evidence of a very cogent kind in favour of Darwin's doctrine of evolution as sufficient to explain "the coming into being" of some types or forms of specific diseases.[47] It therefore appears to me, as it has done to others, that all the weight of *a priori* evidence tends to show that in disease, as in Nature generally, evolution results in the origin of new diseases; that perturbations of the physiological life may ultimately acquire an independent or autonomous existence, so that common disorders may ultimately acquire specific power.

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[46] *On Evolution in Disease.*

It also appears to me that, like erysipelas and diphtheria, the weight of evidence is in favour of the original and occasional *de novo* origin of enteric fever, yellow fever, and typhus fever by "progressive development" through as yet unknown and undetermined factors in the surroundings of the individual—his environment in the widest sense of the term, and that such *de novo* origin does not exclude the possibility of subsequent spread by contagion.

When viewed in the light of our knowledge of the whole world of biology (of which human physiology is but a very small part), the meaning of the facts to which I have referred is unmistakable; and, having regard to pathology as a part of biological science, it will be seen that Darwin's theory of evolution is not inapplicable to its needs; that it is a theory which is capable of explaining much in pathology, when viewed from a biological standpoint, that otherwise and hitherto has not been capable of explanation. It appears, therefore, that "the problem of evolution, in its application to pathology, is to show how the complex, the differentiated, the heterogeneous, have come from the simple, the undifferentiated, the homogeneous; and that some of the present marked types of diseases have slowly arisen by transmutation and descent from, comparatively, a few primordial types; and diseases, like other things, in becoming increasingly numerous, have become more and more different, or, in other words, more complex.[48] The great principle of evolution in pathology stands out clear and firm when the groups of facts relating to disease are considered in co-relation to each other—such facts, for example, as are related to the mutual affinities of diseases in the same group—to the geographical distribution of diseases in past and present times; to their succession and progressive evolution in epidemics; to their progressive development, with increasing definiteness and differentiation, combined with increasing complexity—as slowly evolved in time and space from simpler forms by slow and gradual modifications, through varying elective affinities.

In all cases the process of evolution of diseases implies a succession of changes in the combination of their phenomena, or in the character and grouping of the phenomena, by which one disease passes into another, step by step, from an extreme simplicity or relative homogeneity to a greater degree of complexity or heterogeneity. It has been shown that the variations of diseases from well recognised types are extremely frequent and numerous—that the combinations of morbid phenomena or symptoms presenting themselves always in the same concourse or succession are not always uniform—that cases run by insensible gradations from one type into another. We also see diseases perceptibly getting milder and milder, weaker and weaker, and that they become rarer and rarer as they tend to become extinct altogether, just as races of mankind do. Such has been the case with plague, typhus fever, ague, and dysentery in this country. And although our ignorance of the laws of variation is profound, gradation is shown to prevail from extreme simplicity to great complexity in many diseases of the constitutional and zymotic class, and in their relationship to each other; and to some extent we have also seen that their variations admit of being classified. This recognition of gradation is the first step towards the acceptance of the doctrine of evolution in disease, although the nature of all the physiological factors to which the evolution of diseases may be due is still an open question.[49] "It is these continuously minute differentiations and integrations which constitute evolution."[50]

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[47] "Darwin's Doctrine of Evolution in Explanation of the Coming into Being of some Diseases," by William Aitken, M.D., F.R.S., in *Glasgow Medical Journal*, 1885-86.

[48] Dr. J. Hughlings Jackson, F.R.S., Bowman Lecture, in medical journals of November 21st, 1883.

Through this process, then, it is contended that "diseases of the type known as specific may arise *de novo;* that diverse diseases may own a common ancestry; that specificity depends on the soil in which the seed is sown, and on which it is subsequently cultivated; that the property of contagiousness or infectiveness, dominant in every inflammation and fever, increases in proportion to this specificity, in proportion to successful cultivation on suitable soil; that there is in diseases as in all Nature a tendency of the common to become the specific, the homogeneous to give birth to the heterogeneous; that the distinctive characters of the acute infectious diseases have been and are being progressively built up from an ancestral common fever; and that the relations of the specific fever to common fever have an exact parallel and counterpart in the relation of specific local inflammation to common inflammation; that in anomalous or nondescript cases of disease we are dealing, as it were, with natural variation of species under cultivation.[51]

It is further contended "that in the processes of evolution the living tissue elements of the body itself play a much more important part in the elaboration of septinous and allied poisons than what has been hitherto ascribed to them."[52] "Syphilis, erysipelas, necusia, metria, rubeola, scarlatina, and other zymotic diseases are also seen to put on different forms, which may be referred to the state of the exciter, the mode of its application, the matter on which the exciter acts, or the vitality of the patient, and furnish examples of the changes induced in diseases by the actual constitution of the individual and the mode of infection."[53]

Clinical specificity in disease has been shown to be only partially true. Numerous exceptions or departures from well-known clinical types have been recorded from time to time, alike in constitutional and in zymotic diseases, so that the inevitable questions arise—"How are such cases to be accounted for?" "To what do such cases tend?" and "How do lesser differences or variations become augmented into greater?" "How have species arisen in a state of Nature?" These questions in pathology are equivalent to such a question in biology as is "the origin of species." They are, indeed, but two phases of one question. The anomalous cases of disease cannot any longer be set aside. It may be that they are incipient species, and therefore much greater attention must be given to them than they have hitherto received, so that accurate records as to departures from type should be sought for and obtained, instead of forcible attempts being made to get the records of such cases to conform to type. It is their vagueness or indefiniteness which renders their true nature liable to be overlooked or misunderstood;[54] and in the appropriate language of Sir James Paget they must be made "to probe or to test the rule."[55]

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[49] Compare Huxley, *Coming of Age of the Origin of Species*, p. 348.

[50] Herbert Spencer, *Principles of Biology*, vol. i, p. 80.

[51] Dr. W. J. Collins, *Specificity and Evolution in Disease*, 1884, p. 10.

[52] Surgeon-Major Dr. T. R. Lewis's *Microscopic Organisms Found in the Blood*, Calcutta, 1879, p. 57, and collected works "In Memoriam."

[53] *Vital Statistics*, by Dr. William Farr, a memorial volume edited by Mr. Noel Humphreys, of the Registrar-General's Office, for 1885, p. 247.

I think we have abundant evidence to show that the potentialities of Nature are apt to be underestimated; and we must accept the doctrine in pathology as a part of biology that the laws of variation are ever operative in connection with the origin and development of diseases. Not only does it seem to me that there are good grounds for believing that new diseases are in constantly progressive phases of development, although we may not be able to appreciate them on account of their slowness of evolution, and because in point of time we are living too close to the changes which are constantly going on around us to appreciate their influence sufficiently. "Habitually looking at things rather in their statical than in their dynamical aspects, we never realise the fact that by small increments of modifications any amount of modification may, in time, be generated."[56] There are also grounds for believing that the old diseases are no less constantly being redeveloped side by side with those that are believed to be more widely spread by infection, perhaps because transmission by direct infection may seem to be a more easily recognised cause.[57] As with embryonic development, so with diseases. "I cannot conceive any doctrine professing to bring the phenomena of the former within a general law, which is not like the theory of Darwin, consistent with their fundamental identity, their endless variability, their subjugation to varying external influences and conditions, and with the possibility of the transmission of the vital conditions and properties, with all their variations, from individual to individual, and in the lapse of ages, from race to race."[58]

The eloquent addresses on Pathology to the general meetings of this Association, and to the Section of Pathology during the past ten years, have left me few topics I could make my own, and nothing to say that has not been better said by better men; but it appeared to me that a statement of the position of pathology in relation to biology and to the origin and nature of the specific disease might be of interest, as tending to show that we must continue to look to physiology, through the wide field of biology, as a competent guide for us, and as capable of explaining the abstruse problems still awaiting solution.

If the judicious questioning of received opinions is to be regarded as a sign of scientific vitality and advancement—the very source and root of healthy progress and growth—the Section of Pathology of this great Association of workers during the past ten years may be accepted as evidence of the undoubted vitality of the science of pathology, of advancement in its methods, and of a sound basis for its healthy progress and growth in the future. "All such advances must change the circumstances of our mental life, so that minds that cannot or will not adjust themselves to the changed condition of thought and action become less useful, or at any rate modify the manner of being useful."[59] Seeing, also, that there are no absolute certainties in science—that the conclusions of science are never more than in a high degree probable—that they are no more than the best explanations of phenomena which are attainable in the existing state of knowledge, great advantages accrue from the meetings of such an Association as this throughout its various Sections, where errors are allowed full room for expression, in the belief that truth in the end will prevail, and that in the liberty of opinion, which is the life of knowledge, we ensure the death of what is false. Moreover, in the prosecution of such inquiries as I have here but feebly outlined, every allowance must be made for the opposing influence inspired by that human frailty through which "truth provokes those whom it does not convert." It must also be remembered how difficult it is to get rid of old theories once embraced; and that, whether in pathology or in any other department of science, few are willing to break up trains of thought to which they have been inured.[60] "Emancipation from the thraldom of dogmatic opinion is a slow and difficult process, and the adoption of large and independent views more consistent with observation, reason, and philosophy has only been possible under the influence of the general progress of scientific knowledge, and the acquisition of sounder methods of applying its principles to the explanation of natural phenomena."[61]

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[54] Millican, *loc. cit.*, p. 23.

[55] Paget, Bradshawe Lecture, 1882.

[56] Herbert Spencer, *Elements of Physiology*, vol. i, p. 350.

[57] Darwin's Doctrine of Evolution in Relation to Pathology. By William Aitken, M.D., F.R.S., *Glasgow Medical Journal*, 1885-86.

[58] Dr. Allen Thomson's Presidential Address at the Forty-Seventh Annual Meeting of the British Association at Plymouth.

[59] Sir James Paget, JOURNAL, vol. ii, 1881, p. 196.

To all this the British Medical Association has largely contributed by its organisations in Branches and Sections, by its annual meetings, and by its JOURNAL, where objections reasonably urged always obtain a hearing, where they may be reasonably met, and where new truths, after encountering sufficient opposition to test their value, finally make their way to general acceptance. Out of such a scientific crucible the golden ore of knowledge cannot fail to come out well refined. Moreover, when the opinions of men best able to judge are divided, the questions at issueremain doubtful, and reasonable men who are unable to give special attention to the points at issue withhold their judgment, while those who are able to arrive at conclusions do so with diffidence and modesty, the most fitting frame of mind, holding in remembrance, with Sir Isaac Newton, that "we are diffident in the presence of Nature!"

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[60] Buckle, *History of Civilisation*, vol. iii, p. 415.

[61] Dr. Allen Thomson's Presidential Address at the Forty-seventh Annual Meeting of the British Association at Plymouth.